which underlie it, because his theory assumes that Dalton's law is not valid for the solutions,[1] and as shown above, the hydration theory, which assumes Dalton's law valid and thus contradicts Rothmund's view, explains the observed solubility influences on anhydrides fully as well as does Rothmund's formula, and is further in agreement with the facts on the solubility of hydrates which contradict Rothmund's formula. It is not necessary to assume deviations from Dalton's law to explain these solubility influences, because the usual theory of dilute solutions predicts them mathematically as the result of the changes in the hydration of the dissolved substances which follow the addition of foreign substances to the solution. This hydration theory predicts no reciprocal solubility relation such as Rothmund's formula, and explains the solubility effects by an entirely different cause, the existence of hydrates in solution.

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[CONTRIBUTION FROM THE BUREAU OF CHEMISTRY, U. S. DEP'T OF AGRICULTURE.]

THE SIGNIFICANCE OF CERTAIN NUMERICAL RELATIONS IN THE SUGAR GROUP.[2]

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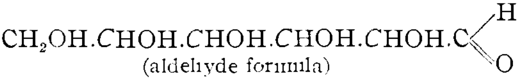
Contents: (1) Introduction; (2) The Theoretical Basis of the Relations and Their Experimental Proof; (3) An Empirical Relation among the Equilibrium Constants of the Mutarotating Sugars; (4) A Systematic Nomenclature of the α- and β-Forms of the Sugars and Their Derivatives; (5) Calculations of the Rotatory Powers of Certain of the Sugars and Their Derivatives; (6) The Influence of Temperature on the Equilibrium in Solution between the α- and β-Forms of the Mutarotating Sugars; (7) The Rotatory Powers of the Glucosides; (8) Summary.

1. Introduction.

The selection of a structural formula for glucose which shall epitomize its reactions is one of the older problems of organic chemistry. Of the many formulas that have been proposed only two have withstood the criticisms that have arisen. The reasons that have caused chemists to prefer these formulas need not be repeated here as they have been presented in a very thorough and convincing summary by Lippmann[3] in his two-volume treatise on the chemistry of the sugars. The rival formulas are usually called the aldehyde and lactonic structures and are as follows:



$$CH_2OH.CHOH.CHOH.CHOH.CHOH.C\begin{matrix}\diagup H \\ \diagdown O\end{matrix}$$

(aldehyde formula)

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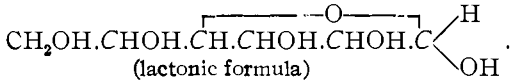
[1] See *Z. Elektrochem.*, **7**, 675, first paragraph; cf. Nernst, *Z. physik. Chem.*, **38**, 489.

[2] Published by permission of the Secretary of Agriculture.

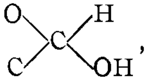
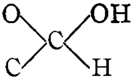
[3] *Die Chemie der Zuckerarten*, 3rd edition (1904), Vol. 2, pp. 1675–1722.

and



$$\mathrm{CH_2OH.}\mathit{C}\mathrm{HOH.}\overbrace{\mathit{C}\mathrm{H.}\mathit{C}\mathrm{HOH.}\mathit{C}\mathrm{HOH.}\mathit{C}}^{\mathrm{O}}\!\!\begin{smallmatrix}\diagup \mathrm{H}\\ \diagdown \mathrm{OH}\end{smallmatrix} .$$

(lactonic formula)

It is to be noted that the lactonic formula, which was first suggested by Tollens, contains one more asymmetric carbon than the aldehyde and accordingly if glucose has the lactonic structure two stereoisomers of it are possible which differ only with respect to the configuration of the end asymmetric carbon, which in the one form has the structure , in the other .

In 1895 Lippmann[1] suggested that the long known mutarotation of glucose may be due to a change from the one lactonic isomer to the other in solution; but as at that time only one form of anhydrous glucose was known, the existence of these stereoisomers was wholly hypothetical. In that and the following year, however, Tanret[2] isolated several new anhydrous modifications of the sugars glucose, lactose, galactose, arabinose, and rhamnose, and the question of the constitution of these new forms revived the discussion of the aldehyde and lactonic formulas for glucose and the other sugars. From the researches which have followed it has been experimentally established[3] that some of the forms which Tanret isolated are mixtures rather than pure substances and at the present time it is practically certain that only three forms of the above-named sugars are known, one of these being a monohydrate and the other two anhydrous modifications. Considerations of valence make it almost certain that the monohydrates of these sugars have the constitution (for glucose)

$$\mathrm{CH_2OH.}\mathit{C}\mathrm{HOH.}\mathit{C}\mathrm{HOH.}\mathit{C}\mathrm{HOH.}\mathit{C}\mathrm{HOH.CH(OH)_2},$$

and thus only the structures of the two anhydrous modifications remain unsettled. E. F. Armstrong[4] and Simon[5] regard these forms as the two possible isomers of the lactonic structure and both have given evidence for this conclusion, that of Armstrong's being particularly convincing. Among other points, he shows experimentally that the α- and β-forms of methyl *d*-glucoside are hydrolyzed by enzymes to methyl alcohol and the α- and β-forms of glucose respectively. As the methyl glucosides show no aldehyde reactions the stereoisomeric lactonic formulas

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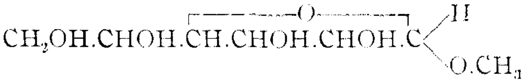
[1] *Loc. cit.*, first edition (1895), pp. 130, 990, 992.

[2] *Bull. soc. chim.* [3], **13**, 728–35 (1895); **15**, 195–205, 349–61 (1896).

[3] In 1902 the author (*Princeton Univ. Bull.*, April; cf. THIS JOURNAL, **30**, 965–6 (1908)) showed that one of Tanret's forms of lactose is a mixture of α- and β-lactoses, and recently Meyer (*Z. physik. Chem.*, **62**, 59–88 (1908)) has proved the same for one of Tanret's forms of glucose.

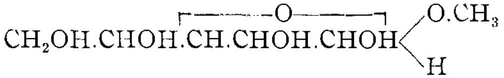
[4] *J. Chem. Soc.*, **83**, 1305–13 (1903).

[5] *Compt. rend.*, **132**, 487–90 (1901).



$$\overbrace{CH_2OH.CHOH.CH.CHOH.CHOH.C}^{O}\begin{matrix}H\\O.CH_3\end{matrix}$$

and



$$\overbrace{CH_2OH.CHOH.CH.CHOH.CHOH}^{O}\begin{matrix}O.CH_3\\H\end{matrix}$$

must be chosen for them[1] and their hydrolysis to the two forms of *d*-glucose indicates that a similar constitution holds for these sugars. Simon has called attention to the fact that the average of the specific rotations of the two anhydrous forms of glucose is 63, which is practically the same as the average for those of the two methyl glucosides, 62; he concludes that this numerical agreement indicates a similarity between the structures of the glucosides and the glucoses.

It is at this point in the discussion that the new facts which are to be presented in the present article enter. The quantitative relation which Simon has noticed can be given a theoretical explanation which leads further to several new relations among the optical rotatory powers of the sugars and their derivatives.

2. The Theoretical Basis of the Relations and their Experimental Proof.

If it be assumed that the two known modifications of glucose are the stereoisomers of the lactonic formula their rotatory powers should be related as follows. Let the rotation which is due to the end asymmetric carbon be A for one isomer, the rotation which is due to its other four asymmetric carbons being B, and the molecular rotation of the whole molecule being thus A + B. The molecular rotation of the other isomer will then be —A + B, since the two isomers are identical except for the end asymmetric carbons and these are antipodes and consequently of equal but opposite rotation.[2] The sum of the molecular rotations of these isomers will accordingly be 2B and their difference 2A. Now consider the molecular rotations of the similar isomers for the other sugars galactose, arabinose, lactose, mannose, etc., all of which contain the same end asymmetric carbon as glucose. It is true that in these sugars the carbon

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[1] Fischer, *Z. Ver. Zuckerind.*, **31**, 66–71 (1893).

[2] It is here assumed that the principle of optical superposition holds for these substances, *i. e.*, that the rotation of the remainder of the molecule is B, irrespective of whether that of the end carbon atom is A or —A. This principle has lately been criticized by Rosanoff (THIS JOURNAL, **28**, 525–33 (1907); **29**, 356–9 (1907)). Although there may be some doubt as to whether the principle holds exactly, it seems to the writer that the experimental evidence on it that has been discussed by Rosanoff clearly shows that it holds closely. Also, it seems quite unlikely that the simple numerical relationships that are shown in the present article, and which are based on the assumption of the correctness of the above principle, could exist if the principle did not hold at least closely. There is certainly a great need for exact experimental evidence on this principle of optical superposition, which is fundamental to the development of stereochemistry.

chain which constitutes one of the groups that is joined to the end asymmetric carbon is not always the same but it appears from the relations which follow that for some reason its variations in the different sugars are practically without influence on the rotatory power of this carbon and that the latter's rotation is closely A and —A respectively for the two forms of all the aldehyde sugars and all their derivatives in which the added substance does not join directly to this end carbon. If the rotation of the other asymmetric carbons in any one of these related sugars be called B′, the molecular rotations of an α and β pair of any one of them will be $A + B'$ and $-A + B'$, and the sum of the molecular rotations will be 2B′, which is different from the sum for the glucoses, but the difference of the molecular rotations will be 2A, which is identical with the difference for the glucoses. It is therefore to be concluded from this theory that *the difference between the molecular rotations of the α and β forms of all the aldehyde sugars and all their derivatives in which the added substance is not joined directly to the end asymmetric carbon atom is a nearly constant quantity.* The experimental proof of this relation is given in Table I, from which it can be seen that though the specific rotations of the various substances vary over a wide range and the sums of the specific rotations also differ greatly, there is a very satisfactory agreement of the differences of the molecular rotations, as is required by the theory. The constant difference may be taken as 16200, and this value will be used in the subsequent calculations in which this constant is used. The fact that the difference for the two forms of *l*-arabinose is a negative quantity, will be explained in the next section along with the reason why I have reversed the usual naming of the arabinoses and called the one of smaller rotation the α form. These points are both related to the fact that arabinose is a levo sugar, that is, one which is genetically related to *l*-glucose, whereas the other substances in the table are all genetically related to *d*-glucose.

TABLE I.

Substance.	Formula.	Molecular wt.	Specific rotation.	Molecular rotation.	Difference.	Sum.
α-d-Glucose[1]	$C_6H_{12}O_6$	180	109	19600	16000	23200
β-d-Glucose[1]			20	3600		
α-d-Galactose[2]	$C_6H_{12}O_6$	180	140	25200	15700	34700
β-d-Galactose[2]			53	9500		
α-l-Arabinose[3]	$C_5H_{10}O_5$	150	76	11400	—16200	39000
β-l-Arabinose[4]			184	27600		
α-d-Lactose[5]	$C_{12}H_{22}O_{11}$	342	86	29400	17400	41400
β-d-Lactose[5]			35	12000		

[1] Roux, *Ann. chim. phys.* [7], **30**, 422 (1903).

[2] Tanret, *Loc. cit.* (1896).

[3] Simon, Quoted by Lippmann, p. 63.

[4] Muller, Quoted by Lippmann, p. 62.

[5] Hudson, THIS JOURNAL, **30**, 1781 (1908).

Consider next those derivatives of glucose in which the addition or alteration affects only the end asymmetric carbon atom, the remainder of the molecule being unchanged. Such compounds are for instance the methyl glucosides, the structural formulas for which have already been given. The unaffected portions of the two forms of the compound will have the same rotations as these portions of the glucoses, namely B, but the end asymmetric carbon will now have the new rotations A′ and —A′ in the two isomers. The molecular rotations of the two forms will thus be $A' - B$ and $-A' + B$ and their difference will be $2A'$ which is no longer equal to the difference for the glucoses, but their sum will be $2B$ and this is identical with the sum for the glucoses. It is therefore to be concluded that *the two isomers of those derivatives of d-glucose in which only the end asymmetric carbon is affected will have molecular rotations whose sum is equal to the sum for the two d-glucoses.* A similar conclusion holds for the similar derivatives of the other sugars, thus the sum for the methyl galactosides must equal the sum for the galactoses, the sum for the ethyl galactosides that for the galactoses and the sum for the ethyl glucosides that for the glucoses. Lastly it may similarly be shown that the differences for the two forms of the methyl alcohol derivatives of all the aldehyde sugars is a constant quantity, and the same holds for the ethyl alcohol and other derivatives, though the constant is in each case somewhat different. The same conclusion probably holds for the phenyl and other

TABLE II.

Substance.	Formula.	Molecular wt.	Specific rotation.	Molecular rotation	Difference.	Sum.
α-*d*-Glucose	$C_6H_{12}O_6$	180	109	19600	16000*a*	23200*b*
β-*d*-Glucose			20	3600		
α-*d*-Galactose	$C_6H_{12}O_6$	180	140	25200	15700*a*	34700*c*
β-*d*-Galactose			53	9500		
α-Methyl *d*-glucoside[1]	$C_7H_{14}O_6$	194	157	30500	36700*d*	24300*b*
β-Methyl *d*-glucoside[2]			—32	—6200		
α-Methyl *d*-galactoside[1]	$C_7H_{14}O_6$	194	196	37900	37900*d*	37900*c*
β-Methyl *d*-galactoside[1]			0	0		
α-Methyl *d*-xyloside[1]	$C_6H_{12}O_5$	164	152	24900	35700*d*	14100
β-Methyl *d*-xyloside[1]			—66	—10800		
α-Ethyl *d*-glucoside[1]	$C_8H_{16}O_6$	208	151	31400	37600*e*	25200*b*
β-Ethyl *d*-glucoside[2]			—30	—6200		
α-Ethyl *d*-galactoside[3]	$C_8H_{16}O_6$	208	179	37200	38000*e*	36400*c*
β-Ethyl *d*-galactoside[4]			—4	—800		

[1] Fischer, *Ber.*, 28, 1145–67 (1895). Natural xylose and its derivatives were considered by Fischer to be genetically related to *l*-glucose, but the recent criticism by Rosanoff (THIS JOURNAL, 28, 114–21) proves conclusively that this is an error, and that natural xylose is accordingly *d*-xylose.

[2] Armstrong, *Loc. cit.*

[3] Fischer and Beensch, *Ber.*, 27, 2481 (1894).

[4] Fischer and Armstrong, *Ibid.*, **35**, 3153.

hydrazones, since the addition in these compounds affects only the end carbon, but the data on the isomeric forms of the hydrazones are not sufficient to permit a quantitative test of the view. In Table II are given the data which prove the above conclusions. Referring to them in order it will be noticed that they hold without exception and quite accurately. In the last two columns letters are appended to the values of the sums and differences in order to show what values should be equal according to the foregoing theory, these equal values being indicated by the same check letter.

3. An Empirical Relation among the Equilibrium Constants of the Mutarotating Sugars.

There is another numerical relation among the rotatory powers of the sugars and their derivatives which, however, seems to be only an approximate empirical relation; in any event it is not founded upon such simple theoretical premises as are the ones that have just been discussed. The α and β forms of the aldehyde and ketone sugars and their derivatives usually establish an equilibrium in solution between the two forms and it is a fact that the ratio of the concentrations of the two forms that are in equilibrium, called the equilibrium constant, has nearly the same value for similar sugars and their derivatives. The equilibrium constant can be calculated from the specific rotations of the pure forms and the rotation of the stable solution in which the forms are present in equilibrium. Thus for glucose the specific rotation of the α form is 109, of the β form 20, of the stable solution 53, hence the ratio of the concentrations of the β and α forms in the stable solution is $\frac{109-53}{53-20} = 1.7$. In Table III are given the equilibrium constants for all the substances upon which the necessary data could be found, and in the last column there is mentioned the solvent in which the substance was dissolved.

TABLE III.

Substance	Specific rotation.		Rotation of stable solution.	Equilibrium constant.	Solvent.
	α-form.	β-form.			
d-Glucose	109	20	53	1.7	Water
d-Lactose	86	35	55	1.5	Water
d-Galactose	140	53	86	1.6	Water
l-Arabinose	76	184	105	0.4	Water
Methyl *d*-glucoside	157	—32	52	1.3	Water
Methyl *d*-galactoside	179	0	82	1.2	Water
d-Glucose pentacetate	4	102	60	1.3	Chloroform
	3	99	57	1.3	Benzene
Ethyl *d*-galactoside	179	—4	?	?	Water
Ethyl *d*-glucoside	151	—30	?	?	Water
Methyl *d*-xyloside	152	—66	?	?	Water

The equilibrium constants for the two hexoses and the disaccharide lactose and the compounds of the hexoses are nearly equal; indeed I doubt whether the accuracy with which the various rotations have been measured is sufficient to show the existence of a real difference in any of these substances. The average value for the equilibrium constant is about 1.5. For the pentose sugar arabinose the constant is quite different from its value for the other substances and it is not likely that this is due to experimental errors because it will be shown later that the other related pentoses, xylose and lyxose, probably also have different equilibrium constants from those of the hexoses. These facts may be summed up by the statement that *the aldohexoses and disaccharides and their compounds have nearly the same equilibrium constant* (1.5). The ketohexoses appear to have other values for the equilibrium constant (see Section 5, under *d-fructose*).

4. A Systematic Nomenclature of the α and β Forms of the Sugars and Their Derivatives.

Since it is clear from what precedes that a close relationship between the α and β forms extends all through the sugar group there can be little doubt that a uniform system of naming these forms by the use of these general relations will be more and more useful as the study of the sugars and their derivatives progresses. Tanret, who discovered the new forms of several of the sugars, gave them the designations α and β apparently upon the plan that the more strongly dextrorotary form should be called α. This system of naming is an arbitrary one and it can be shown that if it is followed in all cases, there will finally result the greatest confusion. Consider the following possibility. The complete antipodal stereoisomer of α-*d*-glucose must have a specific rotation equal and opposite to that for this sugar, accordingly —109, similarly the antipode of β-*d*-glucose must have the rotation —20. Now if the preceding rule is followed the form with rotation —20 must be named α-*l*-glucose since it is more dextrorotary than the other. If this be done it results that the antipode of α-*d*-glucose will be called β-*l*-glucose and that the equilibrium constant for the *d*-glucoses will be the reciprocal for the constant of the *l*-glucoses; there will accordingly be a numerical difference between the values of a corresponding natural constant for two antipodal stereoisomers, *and this* conclusion seems to me an insuperable objection to such a system of naming. It may be said that the rule should be modified so that the more strongly rotating form is called α irrespective of the sign of the rotation, but such a rule would lead to even worse confusion in the case of certain sugars like rhamnose where the α and β forms have different signs of rotation and the exact numerical values are unknown.

The principles upon which a rational and systematic naming of the α and β forms may be based can be obtained from the foregoing stereochemical theory. Starting with *d*-glucose and accepting the present name for its more strongly dextrorotary form, α-*d*-glucose, it is to be observed that the subtraction of the rotation of the β form from that of the α form gives a positive quantity, 16200, and that the sum of the two rotations is also positive. If the naming of the *d*-glucose forms were reversed the sum of the rotations would remain a positive quantity, and this sum for the other sugars would not be identical with the value for *d*-glucose but would vary from sugar to sugar; as the sum is not constant in quantity or sign for the related sugars and does not change sign when the names of the isomers are interchanged it is not a suitable criterion for choosing the names. On the other hand, the difference between the *d*-glucose forms is a constant, 2A = 16200, and depends only on the configuration of the end asymmetric carbon, which is common to all the aldehyde sugars, and changes sign to —2A when the naming of the *d*-glucoses is reversed; accordingly it is as good a criterion as could be desired for naming the forms of the sugars. One point needs to be emphasized, however. If the antipodes of α-*d*-glucose and β-*d*-glucose are named α-*l*-glucose and β-*l*-glucose, and this designation seems satisfactory since it leads to identical numerical values for the equilibrium constants for the respective dextro and levo pairs of the glucoses and has already been used by Fischer[1] in naming the forms of the dextro and levo glucosides, the subtraction of the molecular rotation of β-*l*-glucose from that of α-*l*-glucose will give a negative quantity which is equal and opposite in sign to the similar difference for the *d*-glucoses. The general rule which I desire to propose for naming the α and β forms of the sugars is therefore as follows: *The names should be so selected that for all sugars which are genetically related to d-glucose the subtraction of the rotation of the β form from that of the α form gives a positive difference and for all sugars which are genetically related to l-glucose an equal negative difference.*

According to this rule, since arabinose is derived from *l*-glucose and accordingly named *l*-arabinose though its rotation is right-handed, its form with specific rotation 76 must be named α-*l*-arabinose, the other form of rotation 184 being β-*l*-arabinose. The difference between the molecular rotations of the two forms is then a negative quantity as shown in Table I.

The naming of the two forms of the various derivatives of these sugars should be done with caution, as the above rule, which refers to the sugars, cannot be expected to apply to the derivatives in all cases. Care should be taken to consider the rotations of the two forms of any derivative of the sugars other than glucose in connection with the rotations of the forms of the similar derivative of glucose, the naming of the forms of the glucose derivative being done by the aid of such facts as E. F. Armstrong[2]

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[1] *Ber.*, **28**, 1152 (1895).

[2] *Loc. cit.*

has shown by which it is known for instance that the hydrolysis of α-methyl-glucoside by the enzyme maltase liberates α glucose, which can be distinguished from β glucose by the direction of its mutarotation. It does not seem necessary to enter into the analytical reasoning which leads to the conclusion that can be verified from Table II that the difference between the molecular rotations of the α and β forms of the methyl alcohol derivatives of the sugars which are genetically related to *d*-glucose (*e. g.*, the methyl *d*-galactosides) is numerically the same as the difference for the methyl alcohol derivatives of *d*-glucose and of the same sign, but that for the forms of the similar derivatives of the sugars that are genetically related to *l*-glucose the difference is again numerically equal but now of opposite sign. This conclusion leads to the following rule for naming the forms of those derivatives of the sugars in which the end asymmetric carbon alone is affected, such as the methyl and ethyl alcohol derivatives, the hydrazones, and many of the natural glucosides. *The names of the α and β forms of the derivative of any sugar should be so selected that the difference of their rotations (α—β) is equal to and of the same sign as the difference for the two forms of the similar derivative of that glucose (d- or l-) to which the first sugar is genetically related.* For those derivatives of the sugars in which the end asymmetric carbon is not affected the rule obviously reduces to that given above for the sugars themselves.

5. Calculations of the Rotating Powers of Certain of the Sugars and Their Derivatives.

d-Glucose.—The specific rotation of β-*d*-glucose was given by its discoverer Tanret as 22°. Recently Roux by further purification has reduced this value to 20°. Under such circumstances the substance with the lower rotation must be considered the more nearly pure one but as there is no indication of the amount of the remaining impurity the experiments leave the rotatory power of the pure substance still in doubt. But the relations which are shown in this article agree fairly well with the value 20° and this may accordingly be considered the rotation of pure β-*d*-glucose with a possible error of about two or three degrees.

d-Glucosamine.—It may be that the foregoing relations will explain a curious discrepancy regarding the rotatory power of glucosamine. Hoppe-Seyler and Araki[1] found the specific rotation to be 85, but Lobry de Bruyn[2] only 44 and Breuer[3] 48; Lippmann[4] accordingly considers the first value erroneous. Now the molecular weight of glucosamine is 179 and consequently the difference of the molecular rotations that were found by Hoppe-Seyler and by Breuer is 6600 and their sum 23800. The

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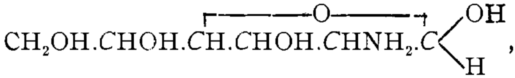
[1] *Z. physiol. Chem.*, **20**, 948 (1895).

[2] *Ber.*, **31**, 2476 (1898).

[3] *Ibid.*, **31**, 2193 (1898).

[4] *Chemie der Zuckerarten* (1904), Vol. I., p. 513.

difference is not at all the same as for the forms of the parent substance glucose but the sum is identical with that for the glucoses which may possibly indicate that these investigators had in hand the α and β forms of glucosamine. Against this view, however, it is to be noted that the usual formula for glucosamine,  $\mathrm{CH_2OH.}\mathit{C}\mathrm{HOH.}\overbrace{\mathit{C}\mathrm{H.}\mathit{C}\mathrm{HOH.}\mathit{C}\mathrm{HNH_2.}\mathit{C}}^{\mathrm{O}}\!\!<^{\mathrm{OH}}_{\mathrm{H}}$, would require the differences to be equal rather than the sums. It seems also probable that as glucosamine has alkaline reaction the equilibrium between its two possible stereoisomers is instantaneously established and that therefore its mutarotation would proceed so fast that when either form is dissolved in water the same rotation would be found. The question obviously requires further experimental investigation.

β-Methyl d-Galactoside.—It is an interesting confirmation of the theory that it requires the rotatory power of this substance to be nearly zero (see Table II). Fischer[1] found that in ten per cent. aqueous solution it showed no rotation. The conclusion must be that this is a substance which is optically inactive or nearly so on account of an approximate balancing of the rotatory powers of the different asymmetric carbons. This conclusion is supported by the fact that Fischer found the substance active in saturated borax solution, which was obviously due to a shifting of the compensating relations.

d-Mannose.—This hexose is known in the solid state as anhydrous crystals[2] of specific rotation —14 three minutes after dissolving, which changes rapidly to become constant in six hours at 14. From the direction of this change it is evident that the other form of *d*-mannose is dextrorotary; its specific rotation can be calculated from the theoretical relations as follows. The molecular rotation of the known mannose form is —(14) (180) = —2500, and since mannose is genetically related to *d*-glucose the difference between the molecular rotations of the two mannose forms must equal and be of the same sign as the difference for the glucoses, 16200; accordingly the specific rotation of the unknown form of mannose is (16200/180) —14 = 76. In agreement with the convention that for dextro sugars the more dextrorotary form is to be named α, this new form is α-*d*-mannose, calculated specific rotation 76, the known form being β-*d*-mannose, specific rotation —14. The equilibrium constant for mannose is calculated to be (76–14)/(14 + 14) = 2.2 which is not far from the value (1.5) found for the other hexoses; as the calculations are based on —14 for the β form and this value is certainly somewhat low since it was found three minutes after dissolving, and as a larger value would cause the equilibrium constant to approach that for the other hexoses,

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[1] *Ber.*, **28**, 1155 (1895).

[2] Van Ekenstein, *Rec. trav. chim.*, **15**, 221–4 (1896).

the agreement may be considered to be as close as the accuracy of the experiments.

d-Maltose.—Only one anhydrous form of maltose has been isolated, specific rotation 119 changing to the constant value 137, which shows that the unknown form of maltose is more dextrorotary and must accordingly be named *α-d*-maltose. Its specific rotation is calculated as for mannose to be 119 + (16200/342) = 166. The equilibrium constant is calculated to be (166–137)/(137–119) = 1.6, which is almost identical with the value found for the hexoses and lactose.

d-Melibiose.—This disaccharide hydrolyzes to *d*-glucose and *d*-galactose and is consequently very closely related to lactose which gives the same products. Its constant specific rotation is 143 and Loiseau[1] found that the freshly dissolved hydrate of melibiose has the specific rotation 124 and the anhydride which was produced by heating the hydrate has the value 146, that of each form changing finally to the above constant value. While the hydrate may have been obtained pure it is quite unlikely that simple drying in the solid state would convert it into the pure lactonic anhydride of the other stereoisomeric constitution, for in the case of the very similar sugar lactose such a transformation has never been accomplished. Choosing therefore the value 124 for the pure hydrate and 143 for the stable solution it is evident that the unknown form of melibiose is more strongly dextrorotary and must be named *α-d*-melibiose, the known form being a hydrate of *β-d*-melibiose. The specific rotation of *α-d*-melibiose is calculated to be 124 + (16200/342) = 171. The equilibrium constant is calculated to be (171–146)/(146–124) = 1.1, which is near that found for lactose, 1.5.

d-Xylose.—This natural pentose is known in only one pure form, initial specific rotation 100, changing to 19 for the stable solution. This change shows that the unknown form of xylose is less strongly dextrorotary and must therefore be named *β-d*-xylose, since this sugar is genetically related to *d*-glucose. The known form is then *α-d*-xylose, specific rotation 100. The specific rotation of the unknown *β-d*-xylose is calculated to be 100 — (16200/150) = — 8. There is a second and independent way by which this specific rotation may be calculated. It has been shown in the theoretical portion of this article that the sum of the molecular rotations of the two *d*-glucoses equals the sum for the two methyl *d*-glucosides and the same reasoning holds for the *d*-xyloses and the methyl *d*-xylosides. The sum for the latter is (see Table II) 14100, therefore the specific rotation of *β-d*-xylose is (14100/150) — 100 = — 6, which is in good agreement with the value found by the other way (—8). The equilibrium constant is calculated to be (100 — 19)/(19 + 7) = 3.3, which is much larger than the value found experimentally for the

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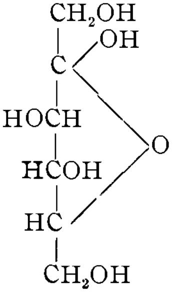
[1] *Z. Ver. Zuckerind.*, **53**, 1050–9 (1903).

related pentose, *l*-arabinose (0.4). The two values are nearly reciprocals.

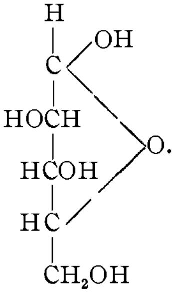
d-Lyxose.—This pentose is known in the solid state in only one form which has the specific rotation —3 taken four minutes after dissolving, and the rotation of the stable solution is —14. The direction of this change shows that the unknown form of *d*-lyxose is less strongly dextrorotary and is accordingly to be called β-*d*-lyxose, the known form being α-*d*-lyxose of specific rotation —3 (approx.). The specific rotation of the β form is calculated to be —(3 + 16200/150) = — 111. The equilibrium constant is calculated to be 0.1, which is smaller than the values for the other pentoses, arabinose and xylose. It seems quite likely that the value —3 for the initial rotation is erroneous and that the pure α form is more dextrorotary than this. Nevertheless the data are quite sufficient to permit the naming of the known form of *d*-lyxose.

l-Rhamnose.—Two forms of this methyl pentose have been isolated by Tanret, of specific rotations 32 and—7 respectively, changing in each case to that of the stable solution 8. The difference of the molecular rotations of the two forms is only —6400, which is so much smaller than the theoretical value —16200 that it seems probable that the substances which Tanret has isolated are not the pure forms but represent only a partial separation. The data, however, permit a naming of the forms. As rhamnose is a levo sugar its levorotatory form is to be called α-*l*-rhamnose, and its dextrorotary form β-*l*-rhamnose; under this naming the difference is a negative quantity as is required by the rule.

d-Fructose.—Only one solid form of this keto-hexose is known, which has the specific rotation —140, the final rotation of the stable solutions being —90. The direction of this change of rotation shows that the other form of fructose is more dextrorotary and is therefore to be named α-*d*-fructose, the known form of specific rotation,—140 being β-*d*-fructose. The specific rotation of the unknown α form of fructose can be calculated as follows. According to Fischer *d*-fructose has the stereo-constitution represented by the lactonic formula



and *d*-arabinose the stereo-constitution



Fructose may therefore be considered a derivative of *d*-arabinose by the replacement of the H of the end asymmetric carbon of the latter by the optically inactive group CH_2OH. The specific rotations of the forms of *d*-arabinose must be equal and opposite to those for the forms of *l*-arabinose which are known to be 76 for the α form and 184 for the β (see Table I). As has been explained in the theoretical portion of this article the sum of the molecular rotations of the two *d*-glucoses equals the sum for the two methyl *d*-glucosides and by the same reasoning it can be shown that the sum of the molecular rotations of the two *d*-arabinoses equals the sum for the two *d*-fructoses. The sum for the two *d*-arabinoses is known experimentally to be $-(76 + 184)(150) = -39000$ (see Table I), accordingly the specific rotation of α-*d*-fructose is calculated to be $140 - (39000/180) = -77$. The equilibrium constant is calculated to be $\frac{90-77}{140-90} = 0.3$, which is in good agreement with the value that has been found for arabinose.

This conclusion that *d*-fructose exists in an α form supports the view that I have expressed[1] regarding the experiments of O'Sullivan and Thompson on the form of glucose that is liberated from sucrose during its inversion by the enzyme invertase. At the time of the experiments of O'Sullivan and Thompson (1890) it was not known that the other product of the inversion of sucrose, *d*-fructose, is a mutarotating sugar, and consequently O'Sullivan and Thompson attributed the decrease of dextrorotation which resulted from the addition of alkali to a solution of sucrose which was undergoing inversion by invertase, to the mutarotation of the glucose alone. Lately E. F. Armstrong[2] has repeated these experiments and has also attributed the decrease of rotation to the glucose entirely since he considers that the mutarotation of fructose is such a slight change in rotation that it may be neglected. Now the fact is that the known mutarotation of fructose is practically as large as that for glucose, it being 50° for the first and 56° for the latter. Such experiments as O'Sullivan and Thompson and Armstrong have performed are indecisive, as the decrease of rotation which they have observed may as likely be due to fructose as to glucose. I have in the above-mentioned article shown how decisive quantitative evidence on this question can be obtained from a simultaneous study of the rate of inversion of sucrose by invertase and the rates of mutarotation of glucose and fructose, and these measurements show conclusively for the first time that the glucose is liberated from sucrose as α-*d*-glucose. Experiments are now being performed to find what form of *d*-fructose is simultaneously liberated.

Certain Stereoisomeric Compound Sugars.—Although the lack of sufficient experimental evidence prevents a thorough discussion of the question it should be mentioned that the stereochemical relations between

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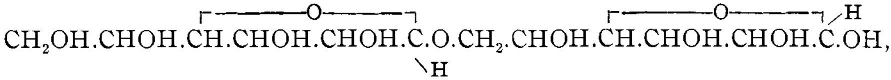
[1] This Journal, 30, 1160 (1908).

[2] *Loc. cit.*

the α and β forms of the hexoses give indications of the structure of some of the disaccharides and higher complex sugars. Thus two of the hexoses, for example glucose and galactose, may unite to form four different disaccharides, each of which will have an α and β form, giving in all eight substances; the formulas of the four disaccharides would be

$$\mathrm{CH_2OH.CHOH.\overbrace{CH.CHOH.CHOH.\overset{H}{C}}^{O}.O.CH_2.CHOH.\overbrace{CH.CHOH.CHOH.\overset{H}{C}}^{O}.OH}$$

and



$$\mathrm{CH_2OH.CHOH.\overbrace{CH.CHOH.CHOH.\underset{H}{C}}^{O}.O.CH_2.CHOH.\overbrace{CH.CHOH.CHOH.\overset{H}{C}}^{O}.OH},$$

the four sugars being possible from these two formulas by the interchanging of the relative positions of the glucose and galactose portions, two of the sugars being thus galactose-glucosides and the other two glucose-galactosides. It seems probable that lactose and melibiose are two of these possible four disaccharides, and the study of the hydrolysis of these sugars by enzymes may be expected to indicate their structures.

6. The Influence of Temperature on the Equilibrium in Aqueous Solution between the α and β Forms of the Mutarotating Sugars.

It has been shown in Section 3 that the equilibrium constants for the aldohexoses and the related bioses all have nearly the same value, 1.5. In the present section new experimental data will be presented which show that the temperature changes the equilibrium in the same sense for all the sugars which have so far been examined, six in number. The method which has been used to determine qualitatively how the equilibrium changes with the temperature, has been described by the writer in connection with an investigation on milk-sugar,[1] and it may therefore suffice to repeat that it consists in cooling quickly a solution of the sugar which has been allowed time to reach equilibrium at a high temperature and observing the slow change of rotation at constant temperature which follows the rapid lowering of the temperature. The reestablishment of equilibrium at the lower temperature is a slow process, and consequently the thermal lag which is noticeable in the optical rotatory power of the cooled solutions is a very certain qualitative indication of the effect of temperature on the equilibrium. The data on the six mutarotating sugars are given in Table IV. The time which elapsed in cooling the solutions from the initial temperature to the final one was in no case more than fifteen seconds, and the change from the initial rotation, which was read about one minute after the solution had reached the lower temperature, to the final constant rotation at this same temperature, took several hours in most cases for its completion. In the sixth column is indicated in each case that form of the sugar which is increased in amount in the

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[1] This Journal, 30, 968 (1908).

solution by a rise of temperature; the conclusion is based on the following reasoning. Referring to glucose it is noticed that the thermal lag in rotation is a 1.8 decrease of dextrorotation, and since the α form of glucose is more dextrorotary than the β form the lag shows that at the higher temperatures from which the solution was cooled the α form is present in excess over the concentration which is stable at the lower temperature. The data show that without exception among the mutarotating sugars which have so far been examined temperature rise favors the α form.

In the seventh and eighth columns are quoted respectively the coefficients of the change of rotation with the temperature of the stable solutions of the sugars, and the form of the sugar which these coefficients indicate as favored by a rise of temperature on the supposition that the change in rotation is due principally to the change of equilibrium. The direct contradiction between many of the conclusions of column eight which are based on this supposition, and those of column six, which seem certainly correct, proves that *the temperature coefficient of the rotation of stable solutions of the mutarotating sugars is not a trustworthy indication of the change in the equilibrium of the mutarotation reaction with temperature.*

TABLE IV.—THERMAL LAGS IN THE ROTATORY POWERS OF THE MUTAROTATING SUGARS.

Substance.	Original temperature.	Final temperature.	Initial rotation.	Final rotation.	Stabler form at high temp's.	Increase of specific rotation per degree.	Stabler form by this coefficient.
d-Glucose	100	25	61.0	59.2	α	0.000	equal
d-Galactose[1]	100	25	49.2	47.0	α	—0.230[2]	β
d-Fructose	100	25	—35.1	—42.8	α	0.620[3]	α
d-Xylose[4]	100	25	8.0	7.0	α	0.036[5]	α
Lactose[6]	100	0	23.3	22.5	α	—0.055[7]	β
Maltose	100	25	79.1	77.5	α	—0.095[8]	β
Sucrose	100	25	52.4	52.4	. .	. . . . .	
Raffinose	100	25	87.3	87.3	. .	. . . . .	
Salicin	100	25	—14.2	—14.2	. .	. . . . .	
Arbutin	100	25	19.8	19.8	. .	. . . . .	

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[1] Heikel (Dissertation, "Ueber die Birotation der Galactose," Kgl. techn. Hochschule, Hannover, 1904) has observed that quickly cooled solutions of galactose in pyridine show a thermal lag in rotatory power, the rotation in one experiment increasing from 3.20° to 5.36°. The velocity of the change of rotation was found to follow the law of unimolecular reactions. These data indicate that in pyridine solution an increase of temperature favors the β-form; in aqueous solution I find the contrary to be the case.

[2] Tanret, quoted by Lippmann, p. 703.

[3] Wiley, THIS JOURNAL, 18, 81–90 (1896).

[4] This is natural xylose, commonly but incorrectly, as pointed out by Rosanoff, called *l*-xylose.

[5] Tollens and Schulze, quoted by Lippmann, p. 127.

[6] THIS JOURNAL, **30**, 968 (1908).

[7] Tanret, quoted by Lippmann, p. 1529.

[8] Meissl, quoted by Lippmann, p. 1471.

In the last four lines of the table are given data regarding experiments to detect a similar thermal lag in the rotation of other sugars and glucosides which do not belong to the mutarotating substances. Not the least indication of such a lag could be detected in these cases; it is evident that the thermal lag is due to the slow establishment in solution of the equilibrium of the reaction which causes the mutarotation, *viz.*, the reversible change between the α and β forms of the sugars.

It may be mentioned at this point that the detection of a thermal lag in the rotatory power furnishes a new method for determining the presence of mutarotation in the case of many sugars for which such a decision has hitherto not been possible. The usual method for detecting mutarotation is to isolate the sugar as a crystalline substance, dissolve the crystals in cold water and seek any slow change in the rotatory power of the freshly prepared solution. This procedure requires that the sugar be crystallizable and it is consequently not applicable to many of the rarer sugars which are not known yet in the crystalline state. On the other hand, the search for a thermal lag in the rotatory power of the solutions requires no crystallization of the sugar and this method is therefore applicable to the rarer syrupy sugars. The writer expresses the hope that it may be possible for those chemists who have in hand preparations of the rarer synthetic sugars to test their concentrated solutions for the presence of thermal lags in the rotatory power. The temperature to which the solution is cooled can advantageously be made 15° or lower, in order that the lag may be as large and slow as possible.

TABLE V.—THE IDENTITY OF THE RATE OF THE THERMAL LAG OF COOLED OR WARMED FRUCTOSE SOLUTIONS AND THE RATE OF MUTAROTATION OF FRESHLY DISSOLVED CRYSTALLINE FRUCTOSE. TEMPERATURE 20°.

A —Mutarotation of freshly dissolved fructose.			B.—Thermal lag of quickly cooled fructose solution.			C.—Thermal lag of quickly warmed fructose solution.		
Time (t) (min.)	Rotation (r).	$\frac{1}{t}\log\frac{r_0-r_\infty}{r-r_\infty}=k$.	Time.	Rotation.	k.	Time.	Rotation.	k.
0	—56.8	...	0	—257.3	...	0	—272.7	...
2	53.6	0.072	2	259.6	0.068	1	271.9	0.067
4	51.4	0.071	4	261.3	0.068	3	270.6	0.068
6	49.7	0.071	6	262.7	0.072	5	269.4	0.077
8	48.5	0.072	8	263.8	0.077	7	268.9	0.070
10	47.7	0.070	∞	265.9	...	∞	267.1	...
∞	45.4	...						
Average		0.071	Average,		0.071	Average,		0.070

The thermal lag is so large in the case of fructose solutions that it has been possible to measure the rate of change of rotation;[1] these measurements show that the change follows the unimolecular reaction formula and that the velocity is exactly the same as that of the mutarotation of

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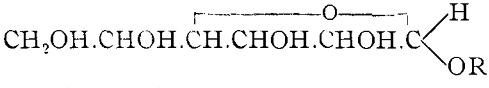
[1] This large lag for fructose was observed at 0° in 1896 by Dr. H. W. Wiley (THIS JOURNAL, 18, 81–90).

freshly dissolved crystalline fructose. The measurements on this lag as shown in Table V include the rate for freshly warmed solutions as well as for freshly cooled ones; the change is seen to be a reversible one and in both cases the velocity is that of the mutarotation. For fructose it is thus clearly proved that the lag is caused by the mutarotation since the two follow the same law and have the same coefficient of velocity.

7. The Rotatory Powers of the Glucosides.

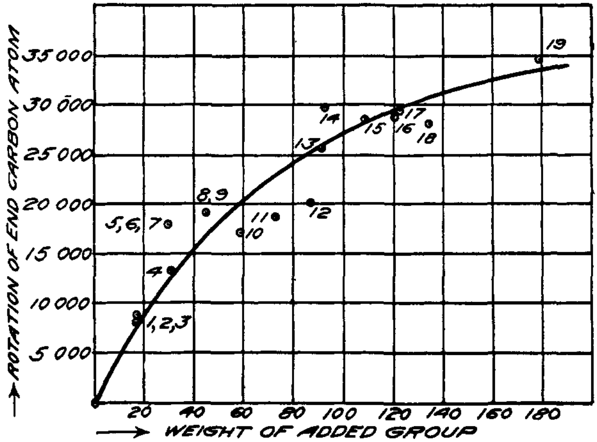
The numerous natural and synthetic glucosides have very similar constitutions and they may nearly all be represented, as proposed by Fischer, by the formula  $\mathrm{CH_2OH.CHOH.\overbrace{CH.CHOH.CHOH.C}^{O}}\begin{matrix}\diagup \mathrm{H}\\ \diagdown \mathrm{OR}\end{matrix}$, where R denotes the group that is combined with glucose to give the glucoside, and which may be, for instance, salicyl alcohol giving the glucoside salicin, coniferyl alcohol giving coniferin, or aniline giving aniline glucoside, etc. The preceding stereochemical theory shows that each of these glucosides is to be expected to exist in two modifications, the α and β forms, depending on the relative space positions of the H and OR groups that are attached to the end asymmetric carbon atom. For the methyl and ethyl glucosides and galactosides and the methyl xylosides these two forms are known, but only one form of the naturally occurring glucosides is known, which in all cases seems to be the β modification, because Fischer has shown that emulsin hydrolyzes only compounds of β glucose, and invertase only compounds of α glucose, and the natural glucosides are all hydrolyzed by emulsin. As the rotatory powers of many of the natural glucosides are known it is possible to calculate the specific rotations of the corresponding α glucosides from the previously discussed relation that the sum of the molecular rotations of a pair of α and β glucosides equals the sum for the α and β glucoses, 23200. Of course this relation applies only to those glucosides in which the R group is not itself optically active; this excludes amygdalin, vicianin, sambunigrin, dhurrin, and amygdonitrilglucoside, and several other cyanogenetic glucosides. If the molecular weight of the known glucoside is W and its specific rotation R_β, the specific rotation of its unknown α form is $R_\alpha = 23200/W - R_\beta$. By means of this formula the specific rotations of the unknown α forms of several of the better investigated glucosides are calculated and given in Table VI.

In these glucosides the group R which is attached to the end carbon atom varies considerably in composition, weight, and structure, and as it is possible to find the rotation of this end carbon atom alone the results serve to show in what manner the rotation changes with the introduction of different groups in the end carbon. It has been shown in Section 2 that the difference of the molecular rotations of the α and β forms of any of the sugars, glucosides, etc., is twice the rotation of the end carbon

TABLE VI.—CALCULATED SPECIFIC ROTATIONS OF UNKNOWN α-GLUCOSIDES.

Substance.	Formula.	Molecular weight.	Sp. rotation of known β form.	Calc. sp. rotation of α form.
Salicin[1]	$C_6H_{11}O_5.O.C_6H_4.CH_2OH$	286	—62	143
Helicin[2]	$C_6H_{11}O_5.O.C_6H_4.COH$	284	—60	142
Arbutin[3]	$C_6H_{11}O_5.O.C_6H_5OH$	272	—62	142
Coniferin[4]	$C_6H_{11}O_5.O.C_{10}H_{11}O_2$	342	—67	135
Phenol glucoside[5]	$C_6H_{11}O_5.O.C_6H_5$	256	—71	162
Urea glucoside	$C_6H_{11}O_5.NH.CO.NH_2$	222	—24	129
Methylurea glucoside[6]	$C_6H_{11}O_5.NH.CO.NHCH_3$	236	—30	128
Dimethylurea glucoside[6]	$C_6H_{11}O_5.NH.CO.N(CH_3)_2$	250	—33	126
Phenylurea glucoside[6]	$C_6H_{11}O_5.NH.CO.NHC_6H_5$	298	—55	146
Aniline glucoside[7]	$C_6H_{11}O_5.NH.C_6H_5$	255	—52	143
Aniline lactoside[8]	$C_{12}H_{21}O_{10}.NH.C_6H_5$	417	—14	114

atom, consequently this rotation is $(R_\alpha-R_\beta)/2$. From this formula the rotation of the end atom is calculated for a number of the sugars and their derivatives as shown in Table VII, and graphically in the accompanying figure, in which the rotations of the end atom are plotted against



Influence of the weight of the added group on the rotatory power of the end carbon atom of the aldose sugars and their derivatives.

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[1] A. A. Noyes and Hall, *Z. physik. Chem.*, **18**, 241 (1895).

[2] Landolt, *Ber.*, **18**, 1600 (1885).

[3] Bourquelot and Herissey, *Compt. rend.*, **146**, 764–6 (1908).

[4] Tiemann, *Ber.*, **18**, 1595 (1885).

[5] Fischer, *Ibid.*, **24**, 28 (1891).

[6] Schoorl, *Rec. trav. chim.*, **22**, 31–77 (1903).

[7] Irvine and Gilmour, *J. Chem. Soc.*, **93**, 1429–41 (1908).

[8] Sorokin, *J. prakt. Chem.* (II), **37**, 304 (1888). For this compound the constant of the preceding formula becomes 41400, which is the sum of the molecular rotations of the α- and β-lactoses, see Table I. From Sorokin's statement, it appears that the aniline lactoside contained a small amount of lactose, and that the observed rotation is therefore slightly too small.

the weights of the introduced groups. The results show clearly that a general relation holds here, for the points lie irregularly about a simple curve which starts from zero rotation when the weight is one (H), the atom being in this case symmetric and consequently inactive, increases with increasing weight at first linearly and then gradually more slowly to become nearly constant for very heavy weights.

TABLE VII.—INFLUENCE OF DIFFERENT GROUPS ON THE ROTATION OF THE END CARBON ATOM OF THE ALDOSE SUGARS.

Diagram number.	Substance.	Molecular weight.	Specific rotation.[1]		Molecular rotation of end carbon.	Weight of attached group.
			α form.	β form.		
1	*d*-Glucose	180	109	20	8000	17
2	*d*-Lactose	342	86	35	8700	17
3	*l*-Arabinose	150	76	184	—8100	17
4	*d*-Fructose[2]	180	—77(*c*)	140	5700	31
5	Methyl *d*-glucoside	194	157	—32	18300	31
6	Methyl *d*-galactoside	194	196	0	18900	31
7	Methyl *d*-xyloside	164	152	—66	17800	31
8	Ethyl *d*-glucoside	208	151	—30	18800	45
9	Ethyl *d*-galactoside	208	179	—4	19000	45
10	Urea *d*-glucoside	222	129(*c*)	—24	17000	59
11	Methylurea *d*-glucoside	236	128(*c*)	—30	18600	73
12	Dimethylurea *d*-glucoside	250	126(*c*)	—33	19900	87
13	Aniline *d*-glucoside	255	143(*c*)	—52	24900	92
13	Aniline lactoside	417	114(*c*)	—14	26700	92
14	Phenol *d*-glucoside	256	162(*c*)	—71	29800	93
15	Arbutin	272	147(*c*)	—62	28400	109
16	Helicin	284	142(*c*)	—60	28700	121
17	Salicin	286	143(*c*)	—62	29300	123
18	Phenylurea *d*-glucoside	298	133(*c*)	—55	28000	135
19	Coniferin	342	135(*c*)	—67	34500	179

A curve of the logarithmic form fits the points of the curve well. Such a curve would follow theoretically from the assumption that the change in rotation due to change in weight of the added group (dr/dw) is proportional to the difference between the rotation (r) and a constant, R, which represents the rotation due to a very heavy group. Thus $dr/dw = a(R - r)$, or integrated under the condition that $r = 0$ when $w = 1$, the equation of the curve is $r = R\ (1 - e^{-a(w-1)})$. The curve of the figure is drawn from this equation using the constants $R = 36000$ and $a = 0.0061$ and employing decimal logarithms.

Summary.

Assuming that the known α and β forms of glucose and the related mutarotating sugars are the two possible partial stereoisomers that are

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[1] The references for the values of the rotations in this table have already been given. The values which have been calculated in the preceding portions of this article are indicated in the table by the letter *c*.

[2] Considered as a derivative of *d*-arabinose, see Section 5.

indicated by the lactonic formula of Tollens, it is concluded that there should exist the following numerical relations among the rotatory powers of these sugars and certain of their derivatives: *1. The difference between the molecular rotations of the α and β forms of all the aldehyde sugars and all their derivatives in which the added substance is not joined directly to the end asymmetric carbon atom is a nearly constant quantity, and (2) The α and β forms of those derivatives* (e. g., *glucosides, etc.*) *of any aldose sugar in which only the end asymmetric carbon is affected have molecular rotations whose sum is equal to the sum for the α and β forms of the aldose.* An experimental test of these conclusions, in which are used the values of the specific rotations that could be found in the literature, confirms them in every case; as they thus appear to be well established they are used in the first place as the basis of a proposed systematic nomenclature for the α and β forms of the various substances, which have heretofore been named arbitrarily, and in the second place to calculate the rotations of some of the sugars and their derivatives which have not as yet been isolated in a pure state. The proposed rule for the naming of the α and β forms of the sugars is: *The names are to be so selected that for all sugars which are genetically related to d-glucose the subtraction of the rotation of the β form from that of the α form gives a positive difference, and for all sugars which are genetically related to l-glucose a negative difference.* The modifications of this rule which are necessary to make it apply to the derivatives of the sugars are discussed and it is concluded that for derivatives in which the end asymmetric carbon is unaffected the rule applies unaltered and for other derivatives it must be restricted as follows: *The names of the α and β forms of the derivative of any sugar should be so selected that the difference of their molecular rotations is equal to and of the same sign as the similar difference for the forms of the similar derivative of that glucose (d- or l-) to which the first sugar is genetically related.* These rules lead to a reversal of the names of the forms of natural (*l*-) arabinose.

The equilibrium constant of the reversible reaction between the α and β forms of the sugars is closely constant (1.5) for the aldohexoses and related disaccharides. This empirical relation permits a calculation of the rotation of the unknown form of several of the sugars which gives results agreeing satisfactorily with those calculated from the foregoing stereochemical considerations.

The thermal lags in the rotatory power of freshly cooled solutions of six of the mutarotating sugars have been observed, and the measurements show that in all cases the α form of the sugar is favored by an increase of temperature. Sugars which do not exhibit mutarotation show no lag. For fructose the progress of the lag has been measured for both quickly cooled and quickly warmed solutions; the lag is reversible, follows the unimolecular reaction formula, and has the same velocity as the mutarotation of freshly dissolved crystalline fructose. It is thus proved to have the same cause as the mutarotation reaction, namely, the slow establishment in solution of the equilibrium between the α and β forms of the sugar.

From the stereochemical theory a formula is deduced which allows the calculation of the rotatory power of the unknown forms of many of the natural and synthetic glucosides. From these calculated values the theory permits a calculation of the influence of the end groups of the glucosides on the rotatory power of the asymmetric carbon atom to which they are attached. The results, which are shown in the figure, indicate that the influence of the group is chiefly due to its weight, and that the rotation of the affected carbon atom changes greatly with the weight for introduced groups of small weight but is constant for those of large weight.

The specific rotations of the unknown α-*d*-fructose and the unknown forms of mannose, maltose, melibiose, xylose, and lyxose are calculated.

[PHOENIX PHYSICAL LABORATORY CONTRIBUTIONS, NO. 17.]

THE CHANGE IN REFRACTIVE INDEX WITH TEMPERATURE. I.

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A considerable amount of work has been done on the determination of the refractive indices of a number of organic liquids at different temperatures.[1] Brühl and W. H. Perkin used this change in refractive index with change in temperature as a means of following the equilibrium between the two forms of certain tautomeric substances. Their results in some instances do not agree.[2]

It was decided, therefore, to attempt to follow these changes more carefully by determining the refractive indices for the sodium and the three hydrogen lines at intervals of 2° or 3° over a range of 50° or 60°, using the purest chemicals obtainable and samples from different sources when possible. In order to be able to judge whether the changes observed with tautomeric substances were normal or not, it was necessary to follow the changes in the refractive indices of other substances with

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[1] Landolt-Bornstein-Meyerhoffer's Tabellen give a very complete summary.

[2] Perkin, in his paper on "Influence of Temperature on the Refractive Power and on the Refraction Equivalents of Acetylacetone and of Ortho- and Para-toluidine," *J. Chem. Soc.*, **69**, 1, concludes with: "It would seem, therefore, that there must be some unnoticed source of error in the refractometer used by Brühl, when it is employed for temperatures somewhat above those of the atmosphere." Brühl in "Studien über Tautomerie," *J. pr. Chem.*, **50**, 192, referring to the fact that the molecular refraction of acetylacetone as determined by Perkin decreased with rise in temperature, whereas his own experimental observations showed it to increase, remarked: "Worauf diese Widersprüche beruhen, vermag ich nicht zu erklären."